UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,578	11/19/2003	Nnochiri N. Ekwuribe	9233.8DV4	6296

20792 7590 09/09/2004

MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

EXAMINER	
GITOMER, RALPH J	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 09/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/716,578	EKWURIBE ET AL.	
	Examiner	Art Unit	
	Ralph Gitomer	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53-60 and 64* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53-60 and 64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The preliminary amendment received 11/19/2003 has been entered and claims 53-60, 64 are currently pending in this application. The claims have been renumbered according to Rule 1.126. The amended title is acceptable. Please update the continuing information in the specification regarding the issue of US 6,703,381. Please comply with all sequence requirements as was previously discussed in the parent application.

The extensive IDS received 11/19/03 has been entered but not considered beyond the single reference submitted, with a date after the present priority date, because the parent application, 09/134,803 is unavailable. Should the file be made available in the future, the examiner will consider any references found in the file.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 53-60, 64 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cetyl-TEG-enkephalin, does not reasonably provide enablement for a peptide conjugate to an amphiphilic oligomer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There is no guidance or direction presented to direct one to determine which such substances would work in the broadly claimed invention which is a complex and unpredictable art. Therefore because of the large number of inoperable embodiments claimed, the ordinary artisan would be subjected to undue experimentation to practice the claimed invention.

The entire scope of the claims has not been enabled because:
1. Quantity of experimentation necessary would be undue because of the large proportion of inoperative compounds claimed.
2. Amount of direction or guidance presented is insufficient to predict which substances encompassed by the claims would work.
3. Presence of working examples are only for a single specific substance and extension to other compounds has not been specifically taught or suggested.
4. The nature of the invention is complex and unpredictable.
5. State of the prior art indicates that most related substances are not effective for the claimed functions.
6. Level of predictability of the art is very unpredictable.
7. Breadth of the claims encompasses an innumerable number of compounds.
8. The level of one of ordinary skill in this art is variable.

In re Wands, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)

On page 47 of the specification, enkephalin conjugates are shown as compared to the active moiety unconjugated and the data would indicate none of the conjugates increase the activity of the moiety at the same dose or for the same period of time. There is a statement of results on page 48 but it is inconsistent with the data presented.

The following is a quotation of the appropriate paragraphs of 35

U.S.C. 102 that form the basis for the rejections under this section made in this

Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 53-60, 64 are rejected under 35 U.S.C. 102(a) as being anticipated

by Ekwuribe.

Ekwuribe (5,681,811) entitled "Conjugation Stabilized Therapeutic Agent Compositions, Delivery and Diagnostic Formulations Comprising Same, and Method of Making and Using the Same" teaches in the abstract, enkephalins and non-naturally occurring opioids are conjugated to lipophilic and hydrophilic moieties. In column 11 a number of drugs are shown which can be conjugated. In column 12 last paragraph, PEG and fatty acids are taught. In column 17 sugars are shown. See the claims.

The present claims are directed to altering the binding affinity of a peptide to its receptor with specific types of compounds that are known to bind to various receptors where the compounds have been conjugated in a particular manner. Ekwuribe teaches the same compounds conjugated in the same manner to be employed for the same function as presently claimed, to bind to receptors. It would be inherent that modifying a compound by conjugating it to a moiety would also alter its binding affinity in some fashion to some degree. The presently claimed compounds are all taught by Ekwuribe for the same function as claimed. The selection of the compound or receptor would not appear to be critical to the invention as claimed.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 53-57, 59-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ekwuribe.

Ekwuribe (6,191,105) entitled "Hydrophobic and Lipophilic Balanced Microemulsion Formulations of Free Form and/or Conjugation Stabilized Therapeutic Agents Such As Insulin" teaches in column 10 lines 31-36, drug conjugates conjugated with a fatty acid group and PEG. In column 16 peptides and proteins are listed that may be conjugated. In column 17 lines 52-55, conjugates may include sugar moieties.

The claims differ from Ekwuribe in that they are directed to a method of altering the binding affinity of a conjugated peptide to its receptor where Ekwuribe teaches administering the same conjugated peptides as claimed for a given function.

It would have been obvious to one of ordinary skill in this art at the time the invention was made to administer the conjugated peptide of Ekwuribe to alter the binding affinity of the peptide because one would have a high expectation of altering binding to receptors by modifying the compounds known to bind to the receptor. Most receptors have a significant degree of specificity in what compounds will bind to them and alterations to those compounds are known to alter their binding.

Claim 58 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Ekwuribe in view of Shashoua.

The claim differs from Ekwuribe in that it is directed to met-ekephalin specifically.

Shashoua (4,933,324) entitled "Fatty Acid Neuroactive Drug Conjugate as a Prodrug" teaches in column 2 lines 53-60, a fatty acid carrier with C16-26 alkyl. In column 14 claim 15 the drug is met-enkephalin.

It would have been obvious to one of ordinary skill in this art at the time the invention was made to administer the conjugated peptide of Ekwuribe where the peptide is met-enkephalin specifically because Shashoua teaches met-enkephalin conjugated in the same fashion as Ekwuribe to be employed as a

drug. One would have a high expectation of success in employing the known closely related compound of Shashoua in the method of Ekwuribe because both are conjugated peptides for binding to receptors.

Claim 64 is rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Ekwuribe in view of Dooley.

The claim differs from Ekwuribe in that it specifies the receptor is an opioid receptor.

Dooley (5,641,861) entitled Opioid Receptor Ligands: Agonists and Antagonists" teaches in the abstract, synthetic amphiphilic opioids.

It would have been obvious to one of ordinary skill in this art at the time the invention was made to administer the conjugated peptide of Ekwuribe to bind to an opioid receptor because Dooley teaches closely related compounds that bind to receptors. In view of the broad classes of peptide compounds taught by Ekwuribe, one of ordinary skill in this art would expect any related peptide to also be effective. The presently claimed synthetic opioids are known to bind to opioid receptors as taught by Dooley.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 53-60, 64 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 56-60 of U.S. Patent No. 6,309,633. Although the conflicting claims are not identical, they are not patentably distinct from each other because the present claims specify altering binding affinity to a receptor where the claims of '633 specify enhanced activity is produced by the same compounds as presently claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 53-60, 64 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of the following applies in all occurrences.

In claim 53 line 1, "the binding affinity" lacks antecedent basis. In claim 54 "characterized in that" is improper and may be intended to be "wherein". Claim 57 contains a Markush group, please confirm that all the members of the group are peptides or proteins. Claim 55 is directed to reducing binding affinity. To reduce the affinity of a peptide would not seem to be consonant with the specification which appears to be seeking compounds with increased binding affinity.

The abstract of the disclosure is objected to because of legal terminology. Correction is required. See MPEP § 608.01(b).

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Ekwuribe (6,703,381) is the parent patent.

Still (US 2003/0104360 A1) teaches synthetic receptor libraries.

Thompson (6,552,170) teaches pegylated peptide compounds.

Anderson (Abstracts Society for Neuroscience), published after the priority date of this application, teaches enkephalins.

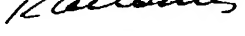
Schiller (5,602,099) teaches synthetic opioids.

Goldstein (4,396,606) teaches synthetic amphiphilic opioids.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ralph Gitomer whose telephone number is (571) 272-0916. The examiner can normally be reached on Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Ralph Gitomer
Primary Examiner
Art Unit 1651

RALPH GITOMER
PRIMARY EXAMINER
GROUP 1200